

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

Figure 1  
 Pharmacokinetics of 40mg Omeprazole Formulations  
 (mean plasma omeprazole concentrations from fasting subjects)

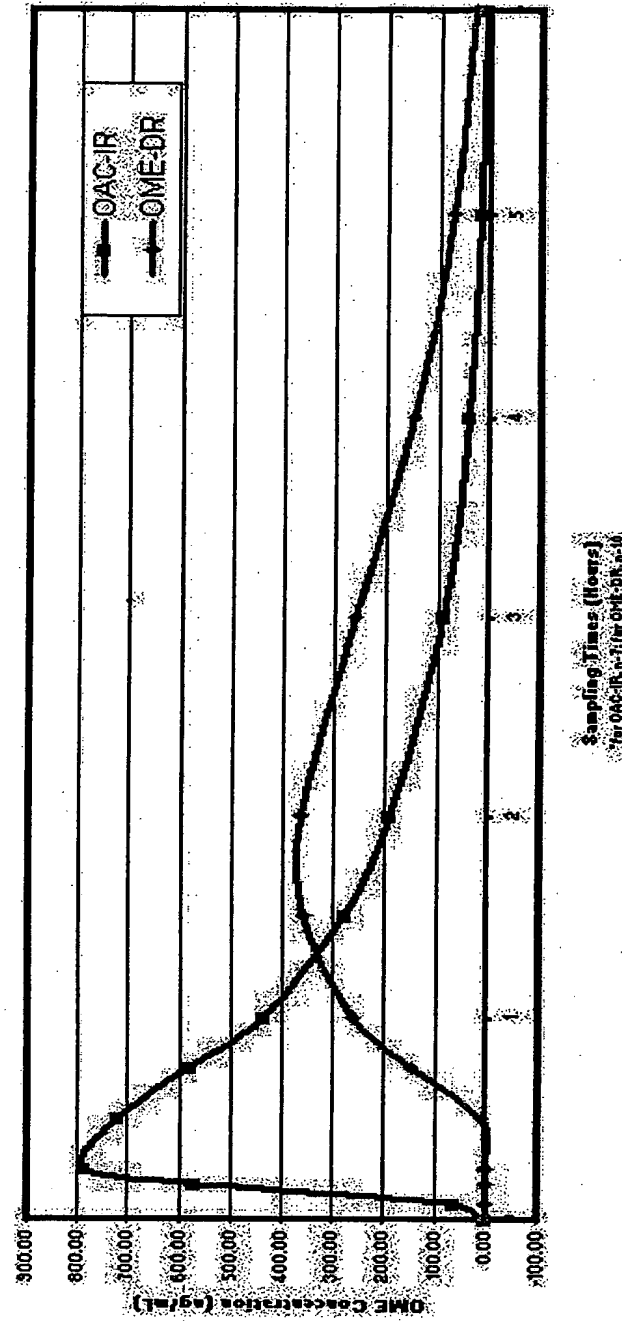
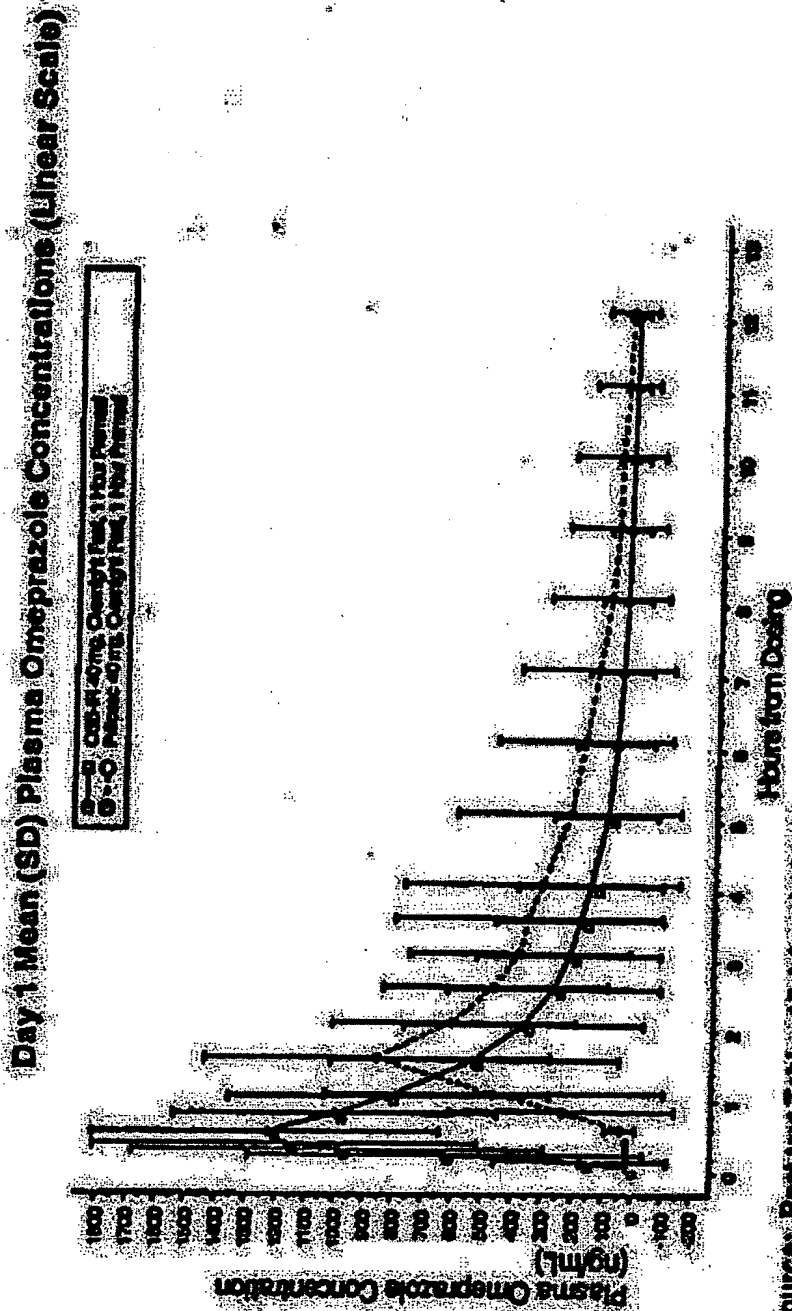


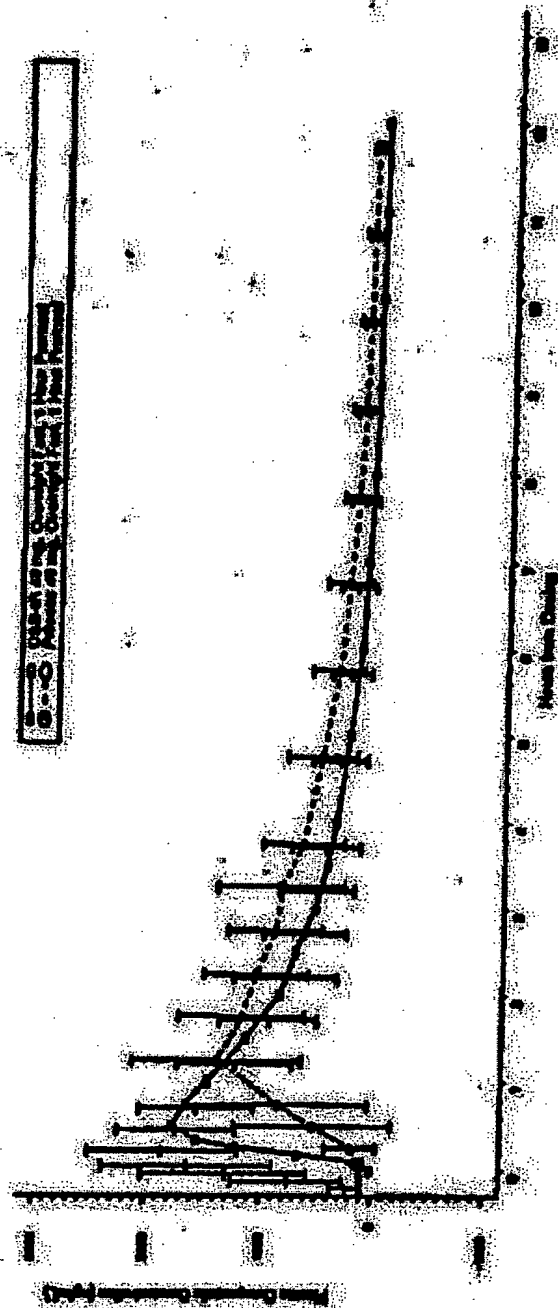
Figure 2



Source: Post-text Tables 15.4.1 and 15.4.4.  
 Notes: The entire curve for Placebo 40 mg treatment is shifted slightly (3 minutes) to the right for ease of reading. Both curves were generated from blood samples taken at the identical time points as indicated for the Omeprazole curve.

Figure 3

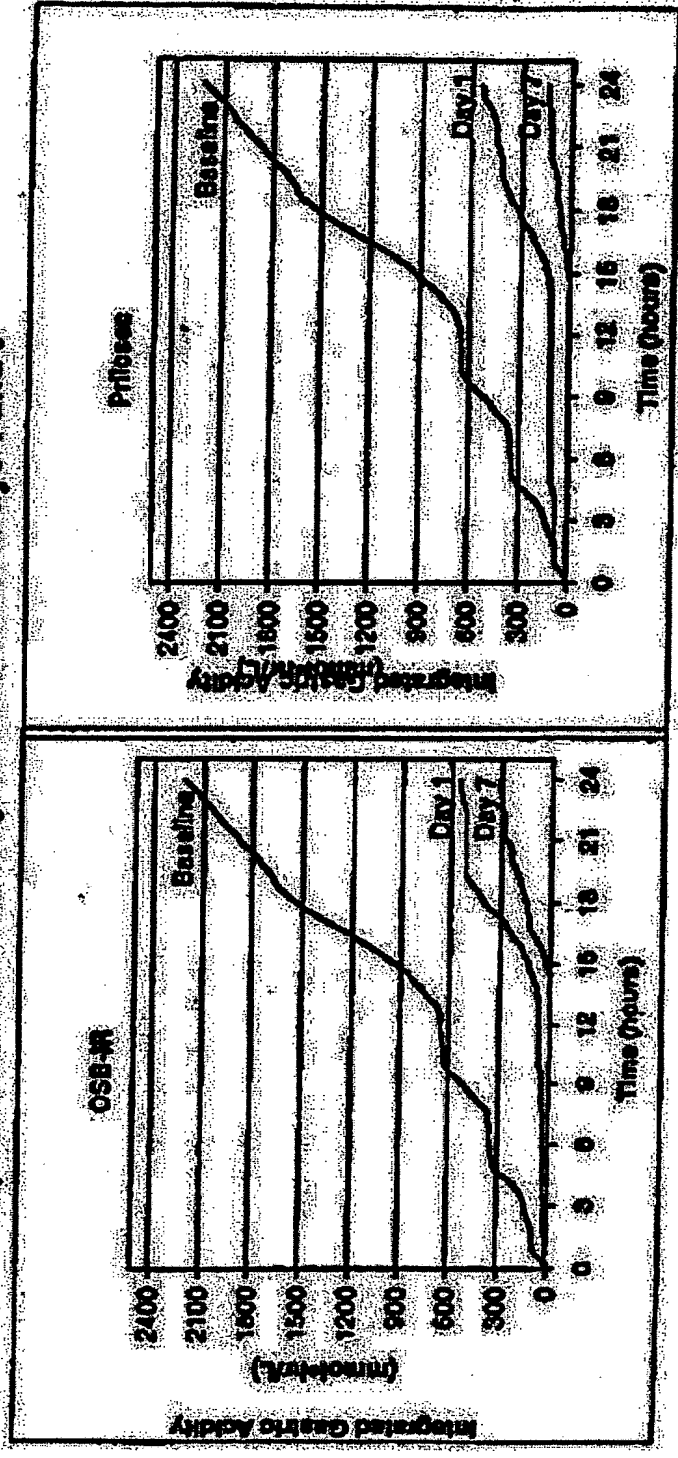
# Day 7 Mean (SD) Plasma Omeprazole Concentrations (Linear Scale)



Source: Post-text Tables 15.4-2 and 15.4-5.1.  
 Note: The entire curve for Prolisec 40 mg treatment is shifted slightly (3 minutes) to the right for ease of reading. Both curves were generated from blood samples taken at the identical time points as indicated for the OSB-IR curve.

Figure 4A and Figure 4B

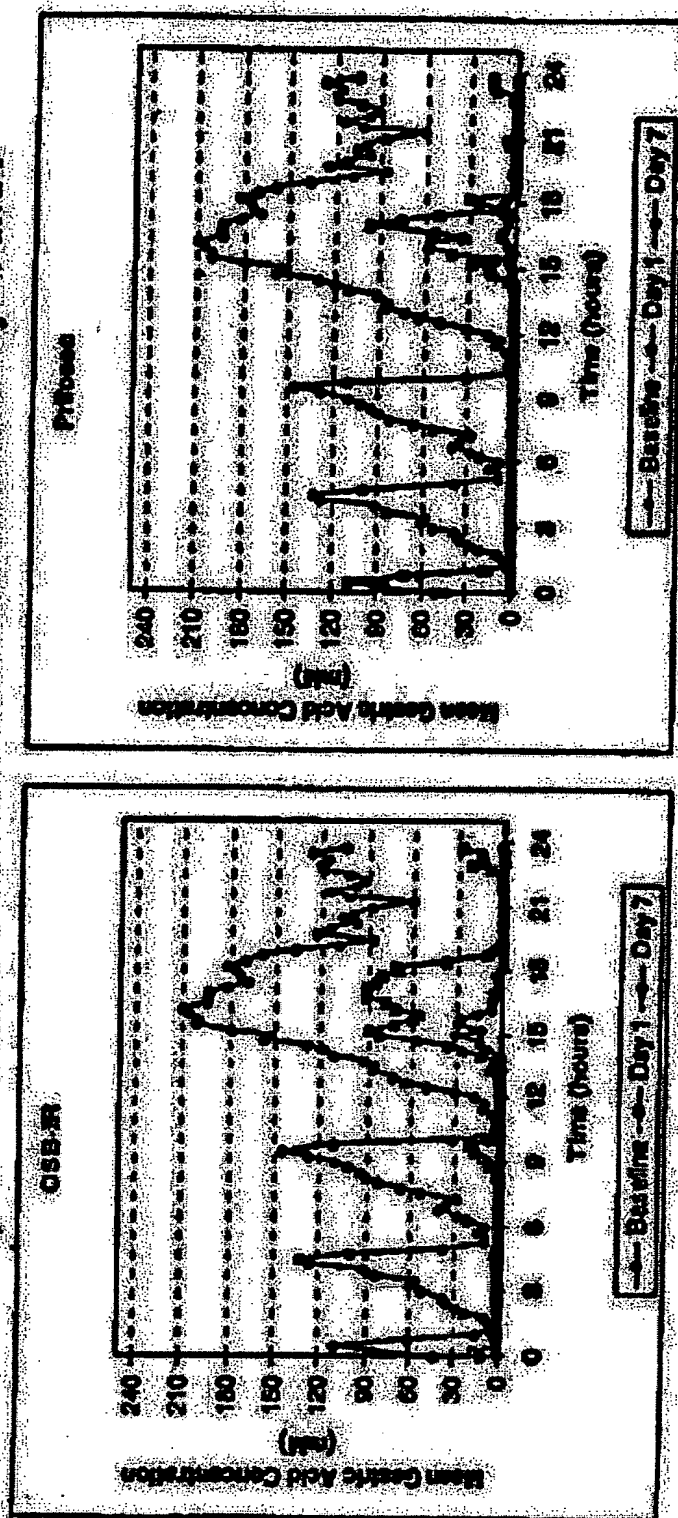
# Integrated Gastric Acidity at Baseline and Days 1 and 7



Note: Zero time is the time of dosing. The time curve was plotted using mean values for the 15-minute time intervals over the 24-hour post-dosing recording period. Baseline values were calculated as means from the two baseline recordings. Results are medians from 24 subjects.

Figure 5A and Figure 5B

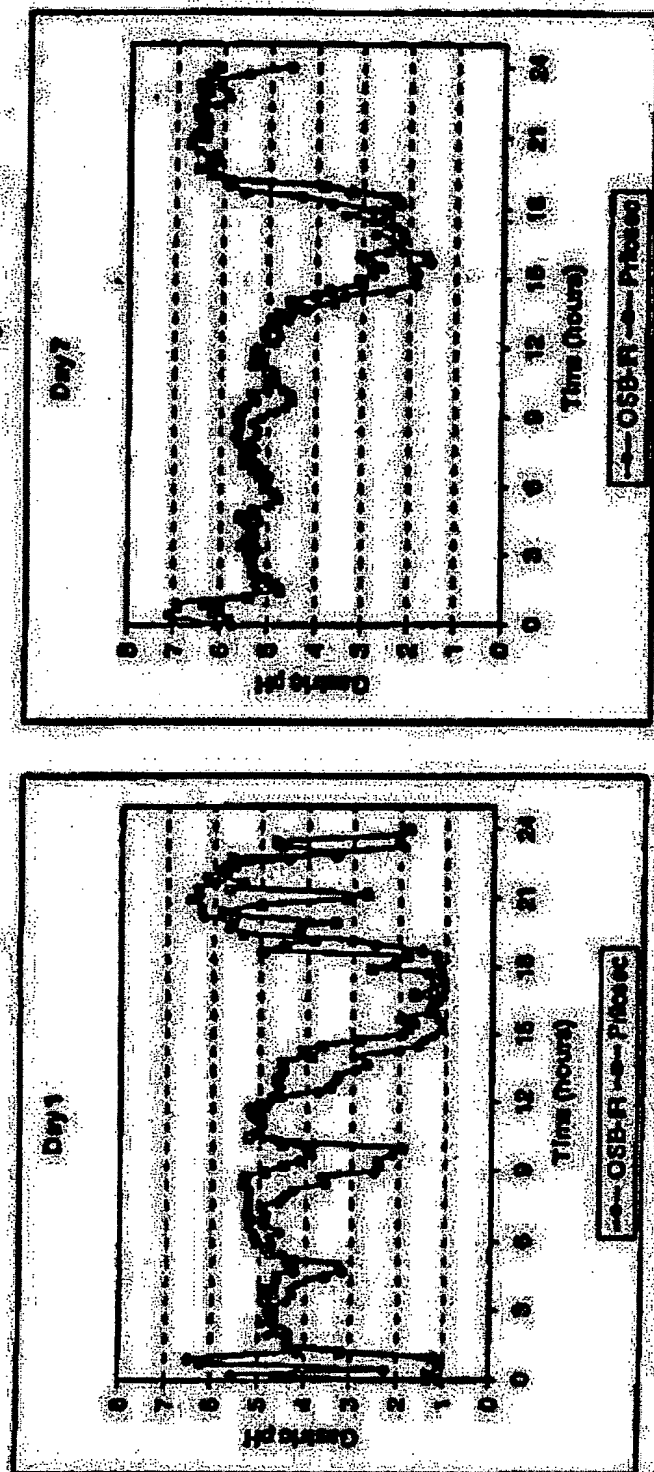
# Mean Gastric Acid Concentration at Baseline and Days 1 and 7



Note: Zero time is the time of dosing. Values are displayed for each 15-minute interval of the 24-hour post-dosing recording period. Baseline values were calculated as means from the two baseline recordings. Results are medians from 24 subjects.

Figure 6A and Figure 6 B

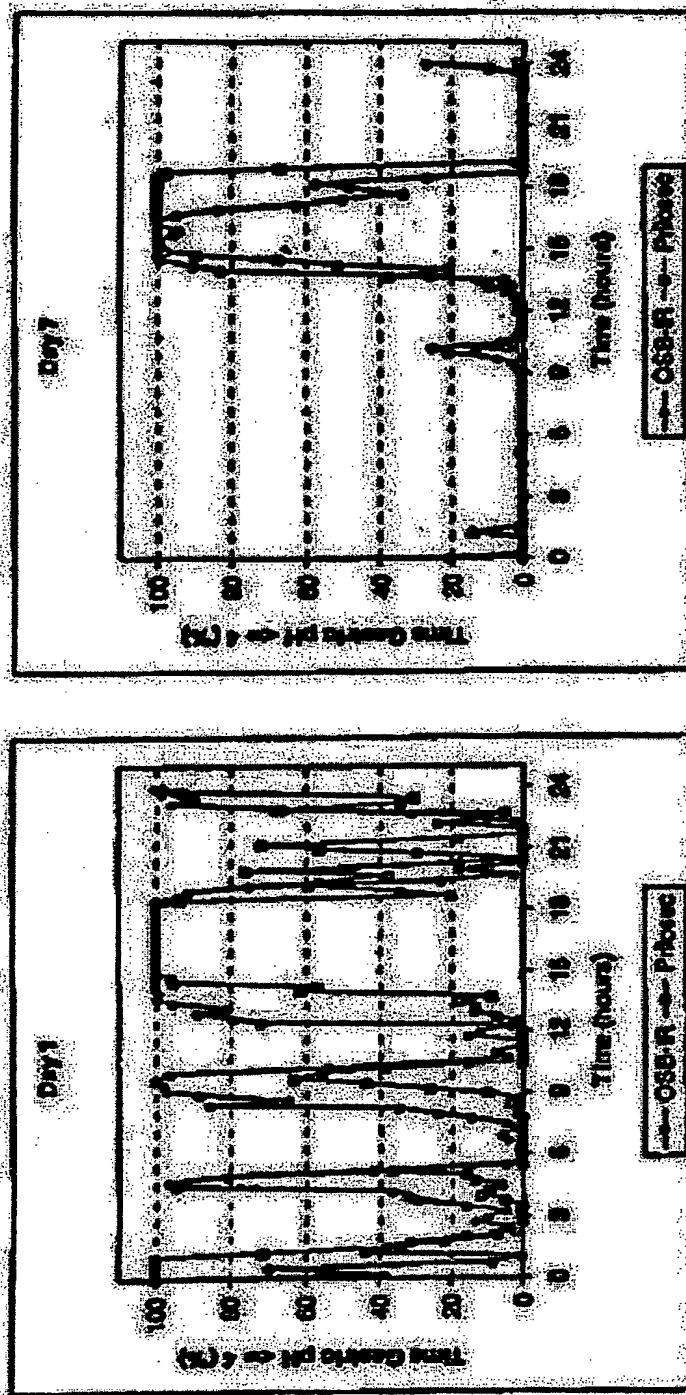
# Median Gastric pH with OSB-IR and PiloSec on Days 1 and 7



Note: Zero time is the time of dosing. Values are displayed for each 15-minute interval of the 24-hour post-dosing recording period. Results are medians from 24 subjects.

Figure 7A and Figure 7B

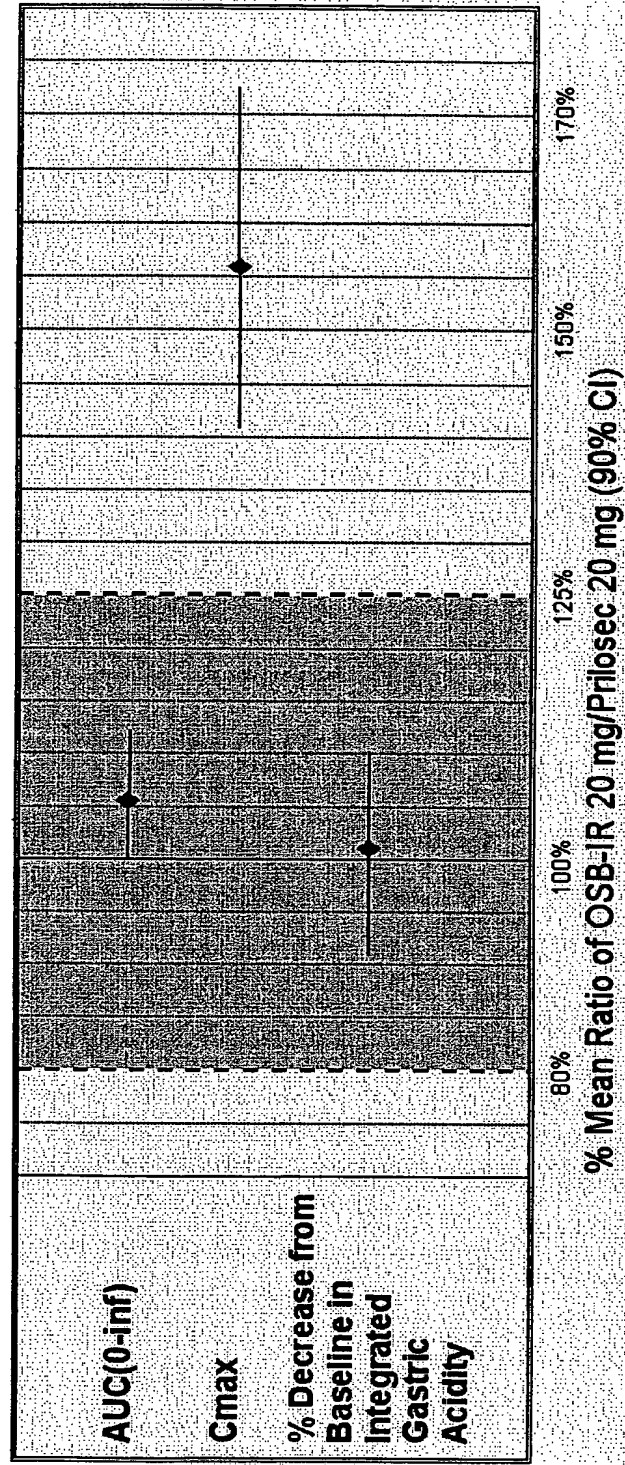
# Time Gastric pH $\leq 4$ with OSB-IR and PiloSec on Days 1 and 7



Note: Zero time is the time of dosing. Values are displayed for each 15-minute interval of the 24-hour post-dosing recording period. Results are medians from 24 subjects.

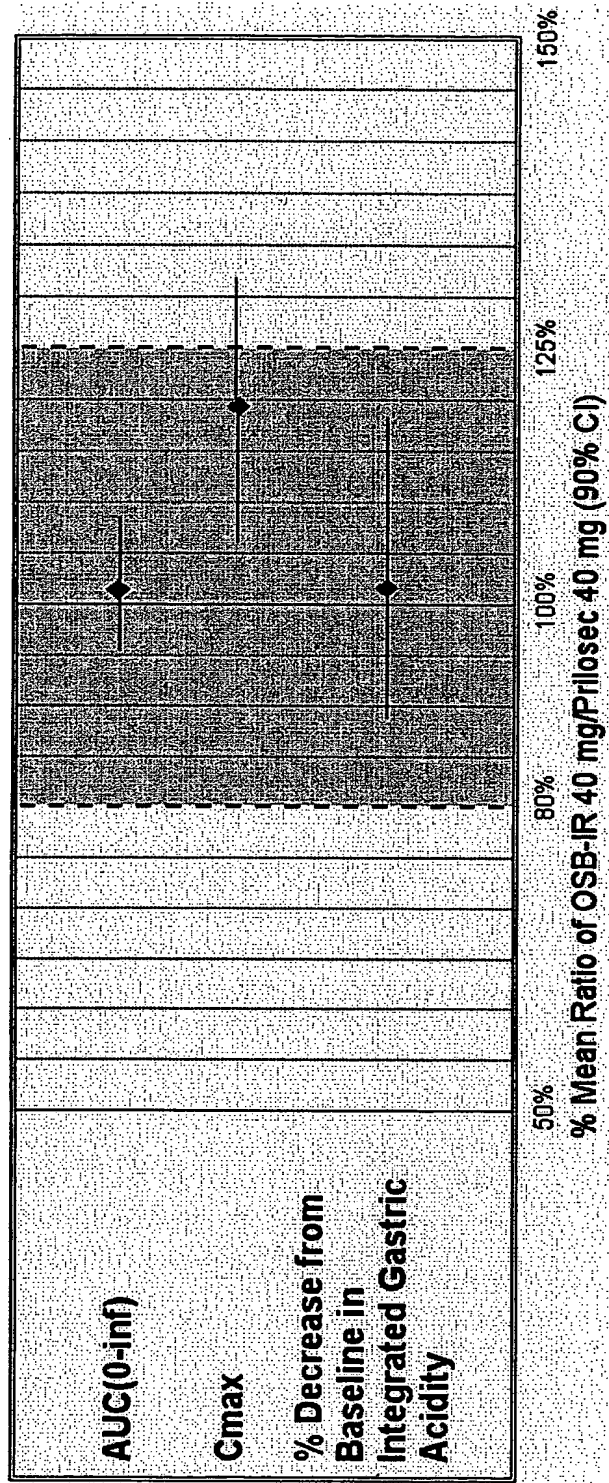


Figure 8A  
Comparison of PK/PD Parameters for OSB-IR and Prilosec® 20 mg



OSB-IR-C06

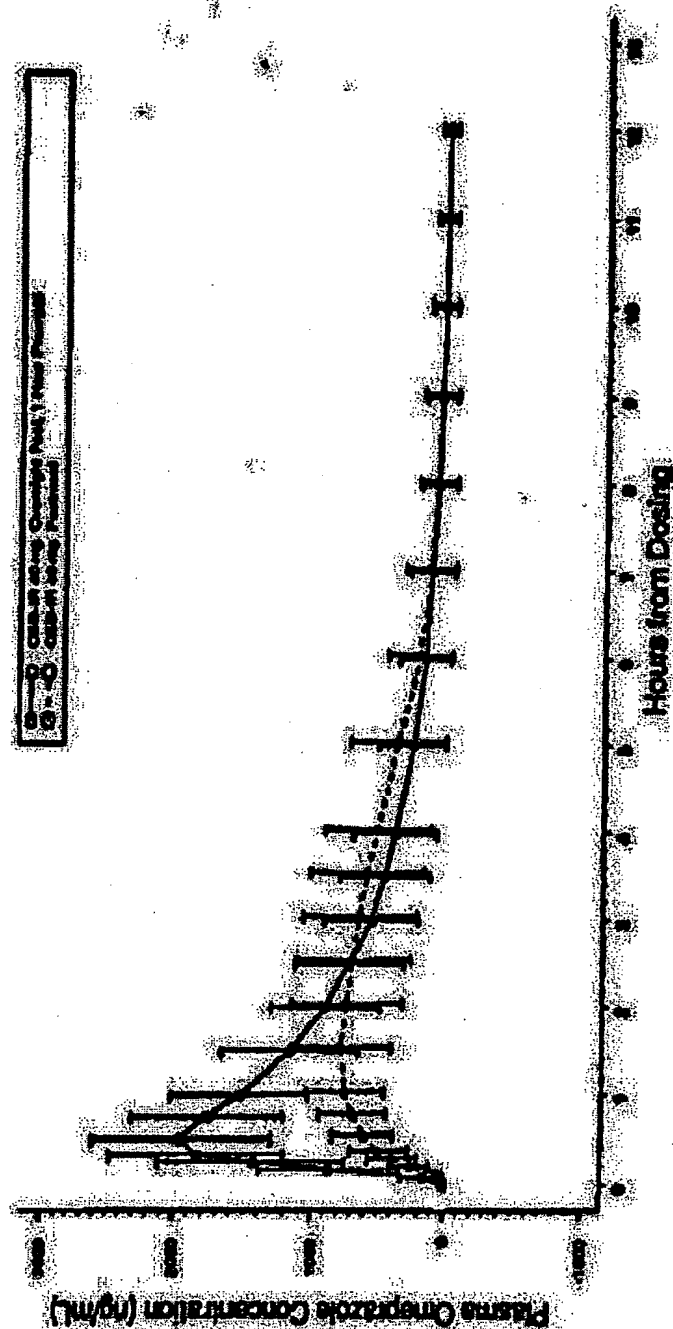
Figure 8B  
Comparison of PK / PD Parameters for OSB-IR and Prilosec® 40mg



OSB-IR-C02

Figure 9

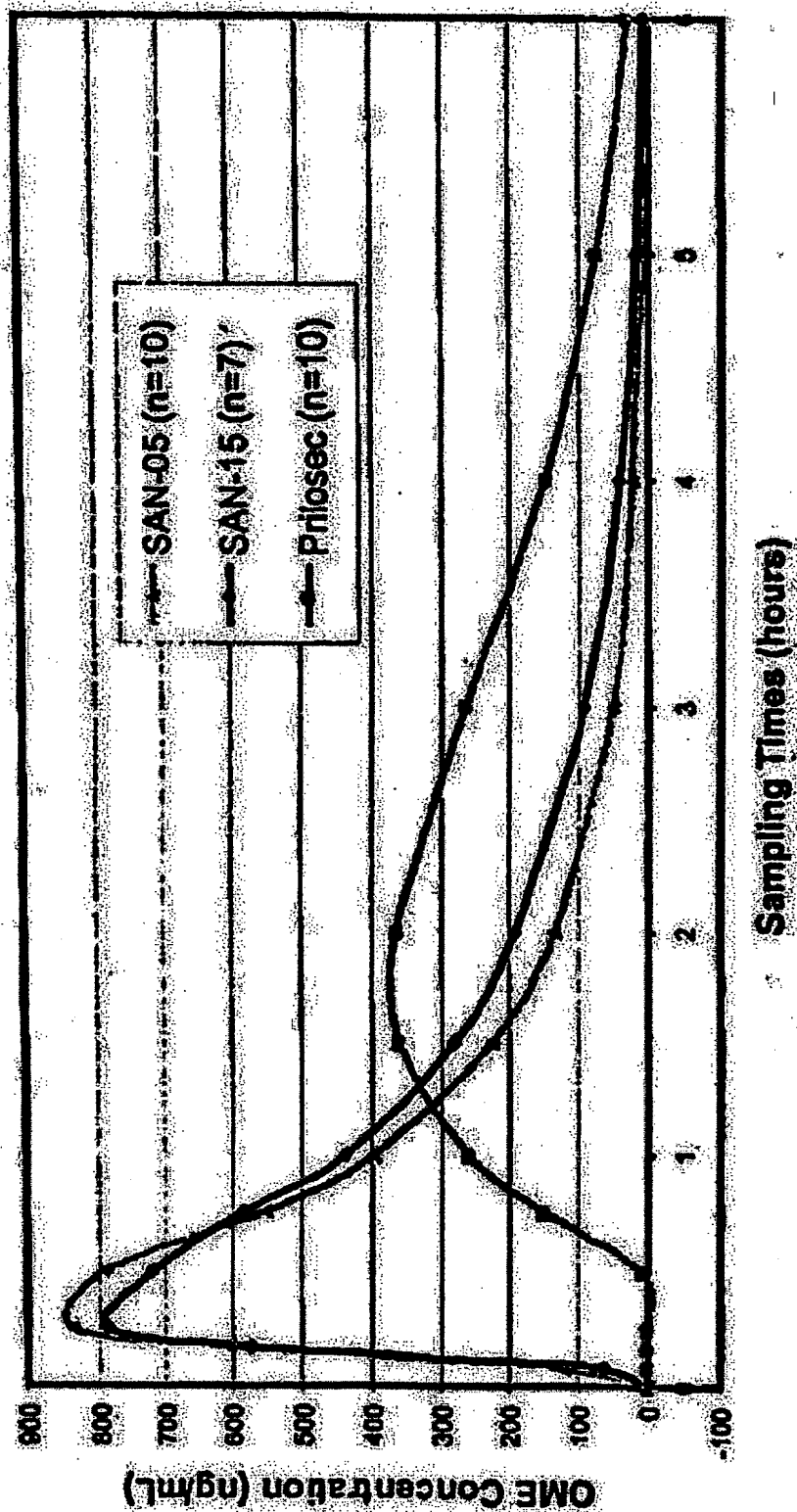
**OSB-IR Postmeal (Day 8) vs Premeal (Day 7) Mean (SD) Plasma Omeprazole Concentrations at Steady State (Linear Scale)**



Source: Post-test Tables 15.4-3 and 15.4-15.

Note: The entire curve for OSB-IR 40 mg. Postmeal treatment is shifted slightly (3 minutes) to the right for ease of reading. Both curves were generated from blood samples taken at the identical time points as indicated for the OSB-IR curve.

Figure 10



mean plasma omeprazole concentrations from fasting subjects

Figure 11

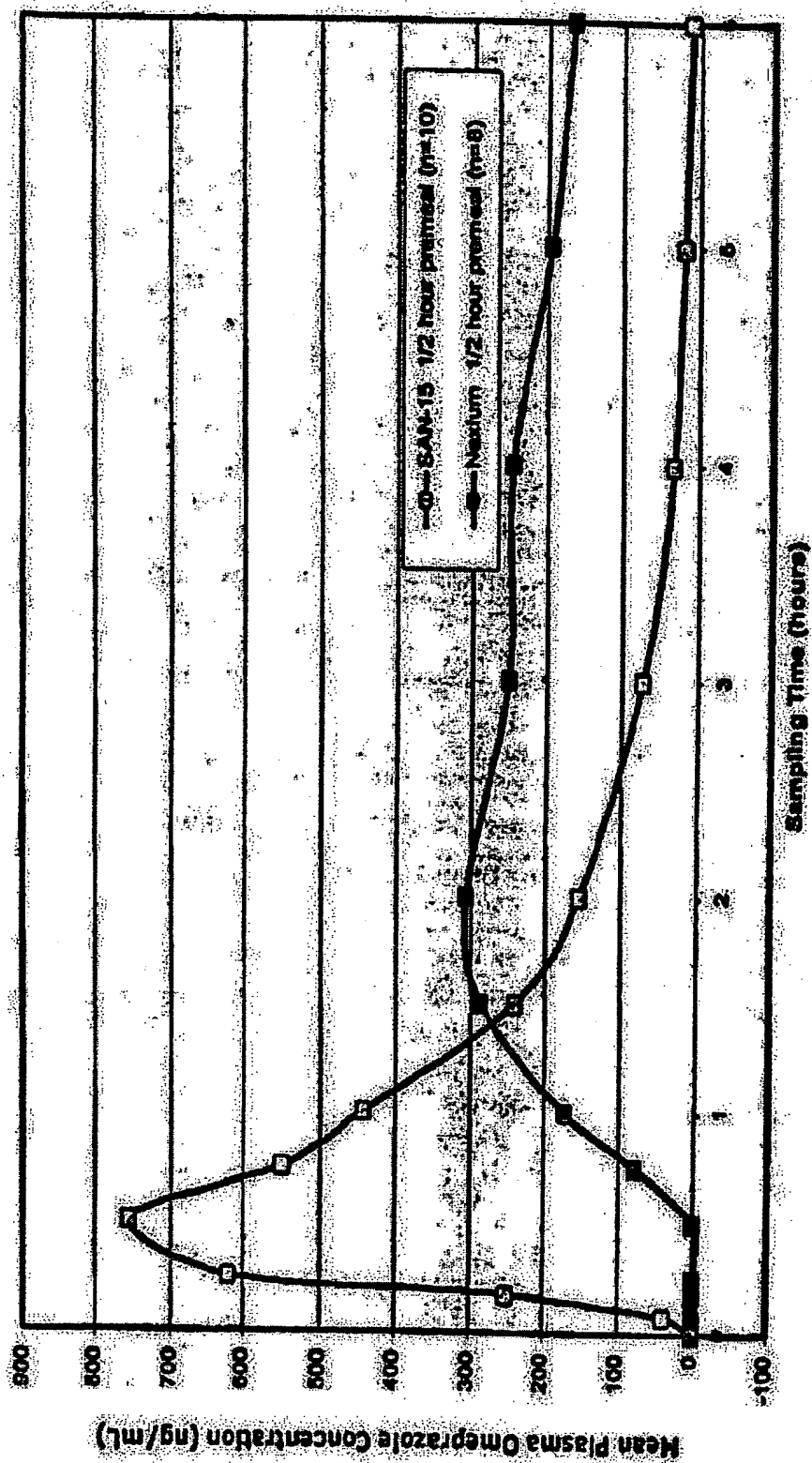


Figure 12

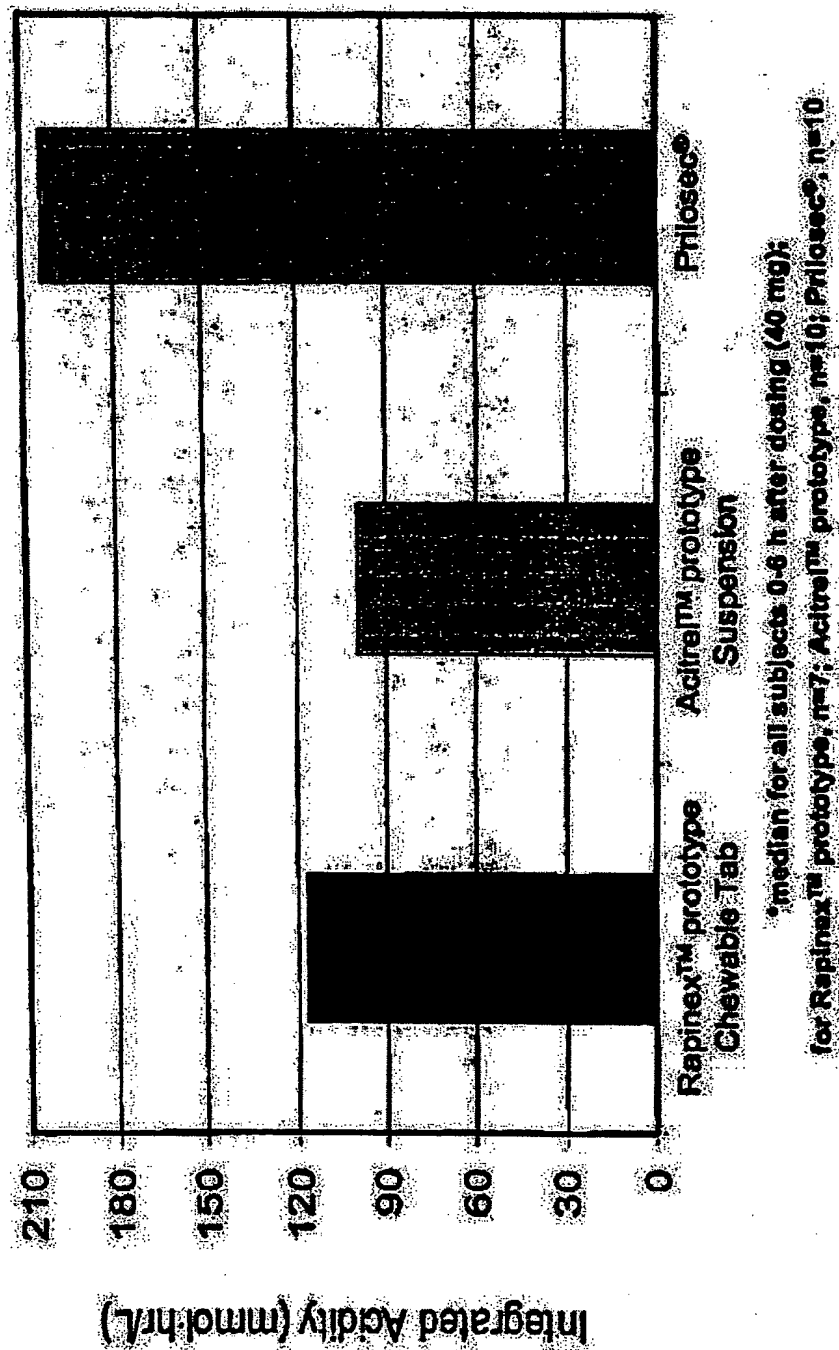
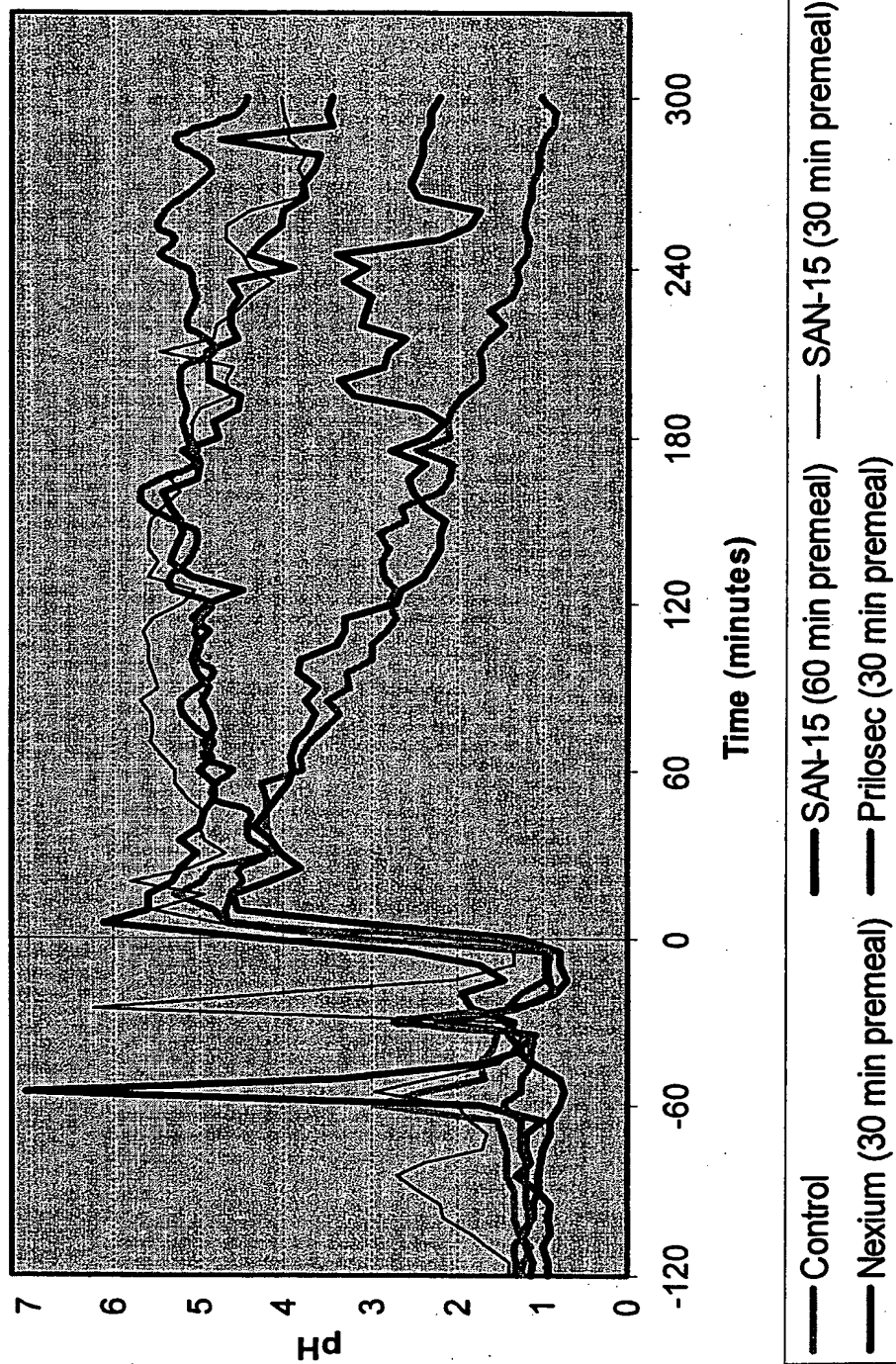
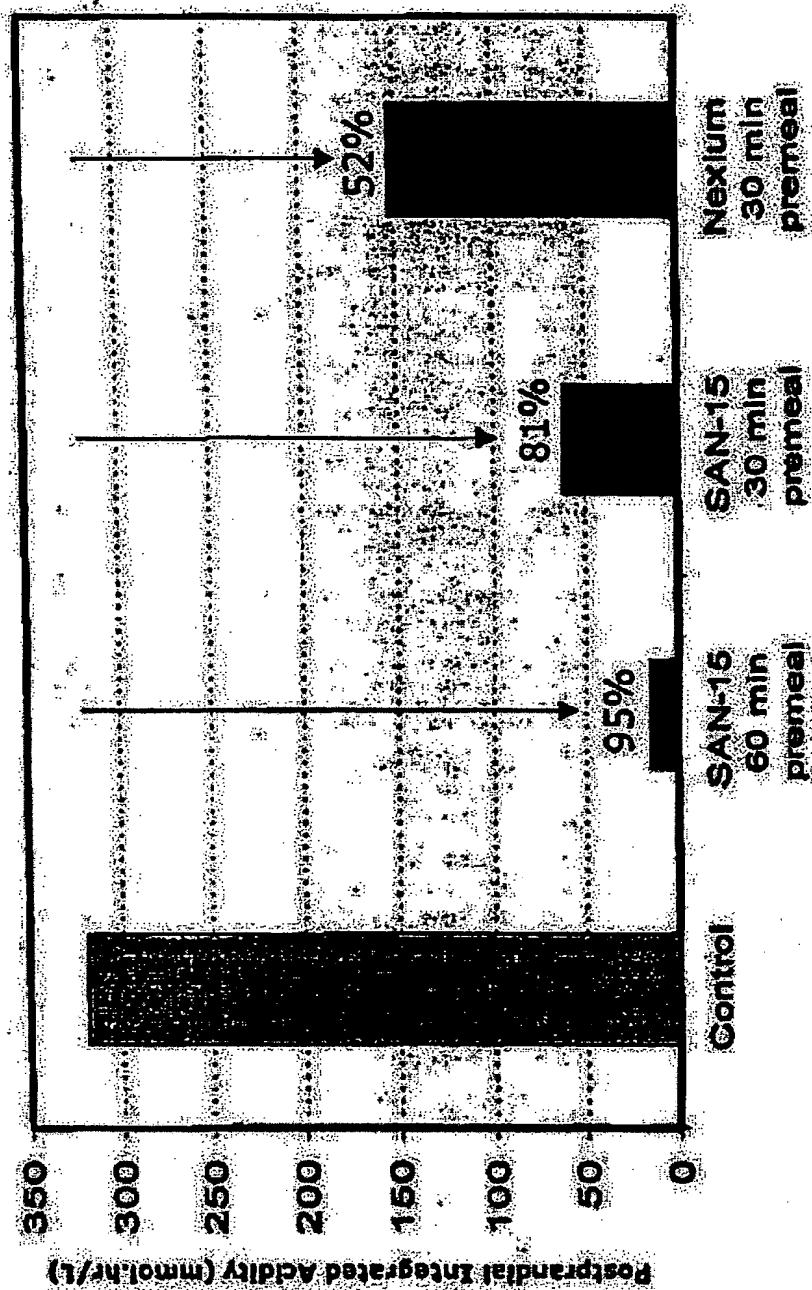


Figure 13  
Effect of Omeprazole 40 mg on Gastric pH\*  
(proximal electrode)



\*median for all subjects; for Control and SAN-15, n=10; for Prilosec and Nexium, n=8

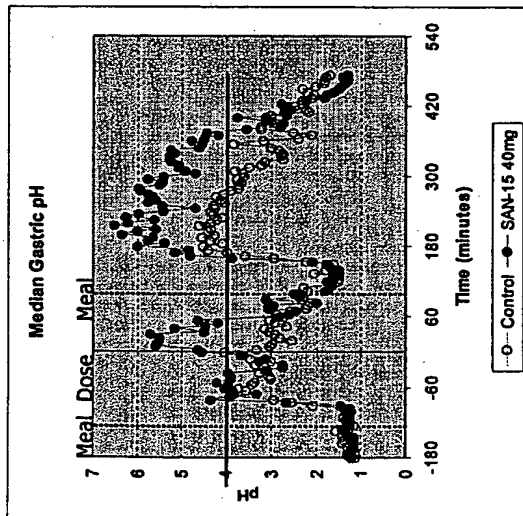
Figure 14



\*Integrated gastric acidity over 210 minutes; median for all subjects; for Control and SAN-15, n=10; for Nexium®, n=8



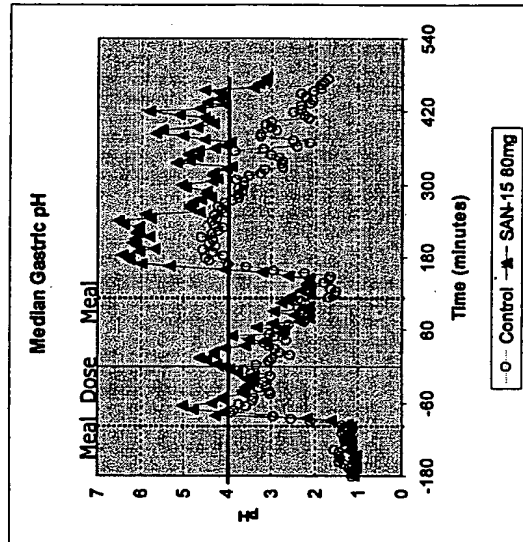
Figure 15A, Figure 15B, Figure 15C  
Dose Response for SAN-15\*  
(postprandial dose)



Mean = AUC(0-t) = 260 ng·hr/mL  
Median = AUC(0-t) = 200 ng·hr/mL

After Meal 2 (160 – 475 min.)

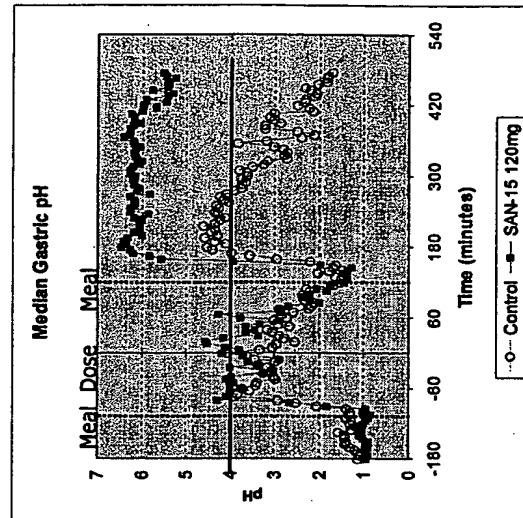
Integ. Acidity : 41.5  
mmol·hr/L  
% Time pH > 4: 52.6%



Mean = AUC(0-t) = 841 ng·hr/mL  
Median = AUC(0-t) = 422 ng·hr/mL

Control Integ. Acidity : 65.9  
mmol·hr/L  
% Time pH > 4: 39.0%

Integ. Acidity : 11.1  
mmol·hr/L  
% Time pH > 4: 71.4%



Mean = AUC(0-t) = 1604 ng·hr/mL  
Median = AUC(0-t) = 790 ng·hr/mL

Integ. Acidity : 0  
mmol·hr/L  
% Time pH > 4: 99.0%

\*Median values  
SAN-15-C01C  
n=10

Figure 16  
Food Effect (premeal dosing) on  
Bioavailability of SAN-15

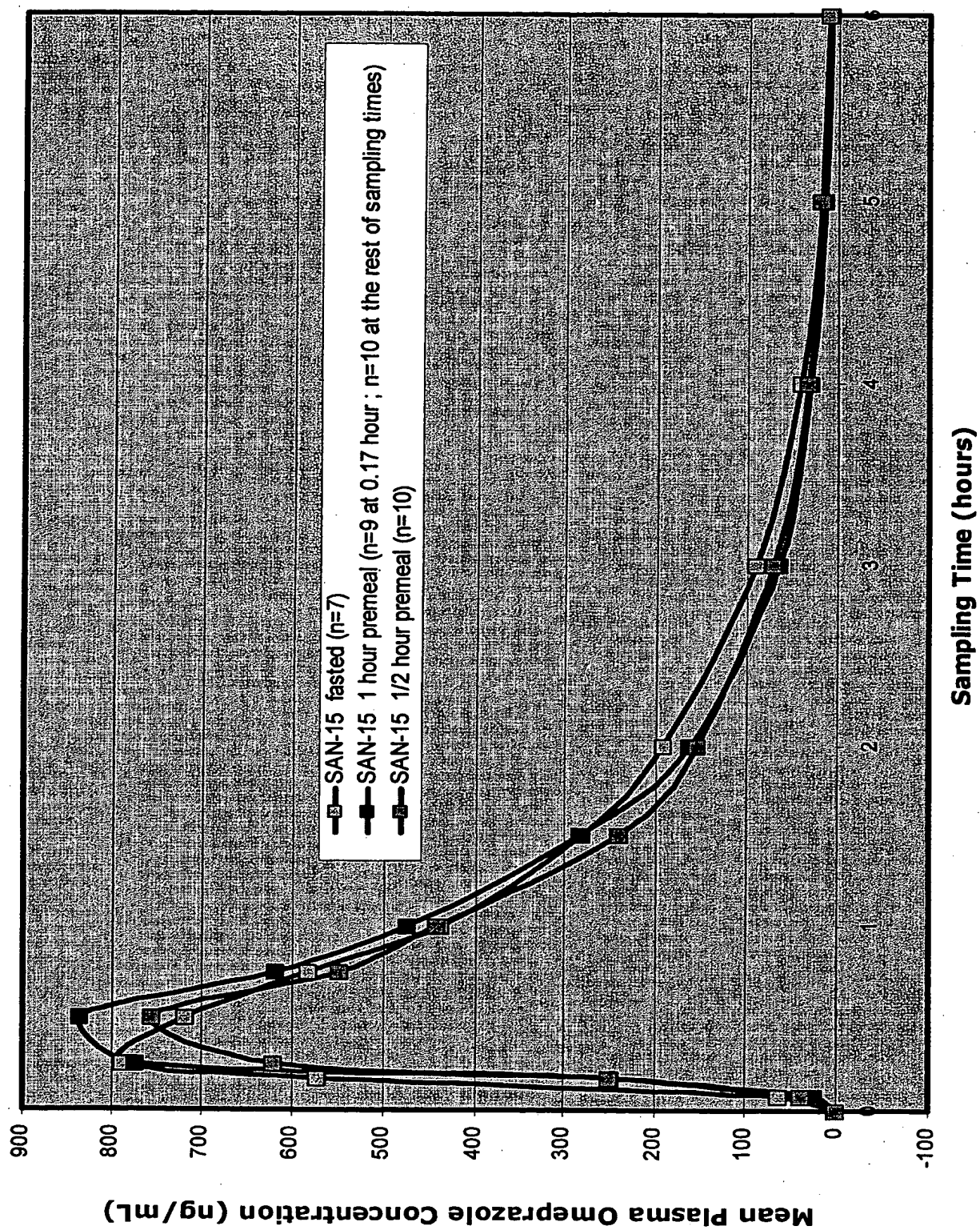


Figure 17

Mean Plasma Omeprazole Concentrations After Two Doses of OSB-IR Suspension 40 mg

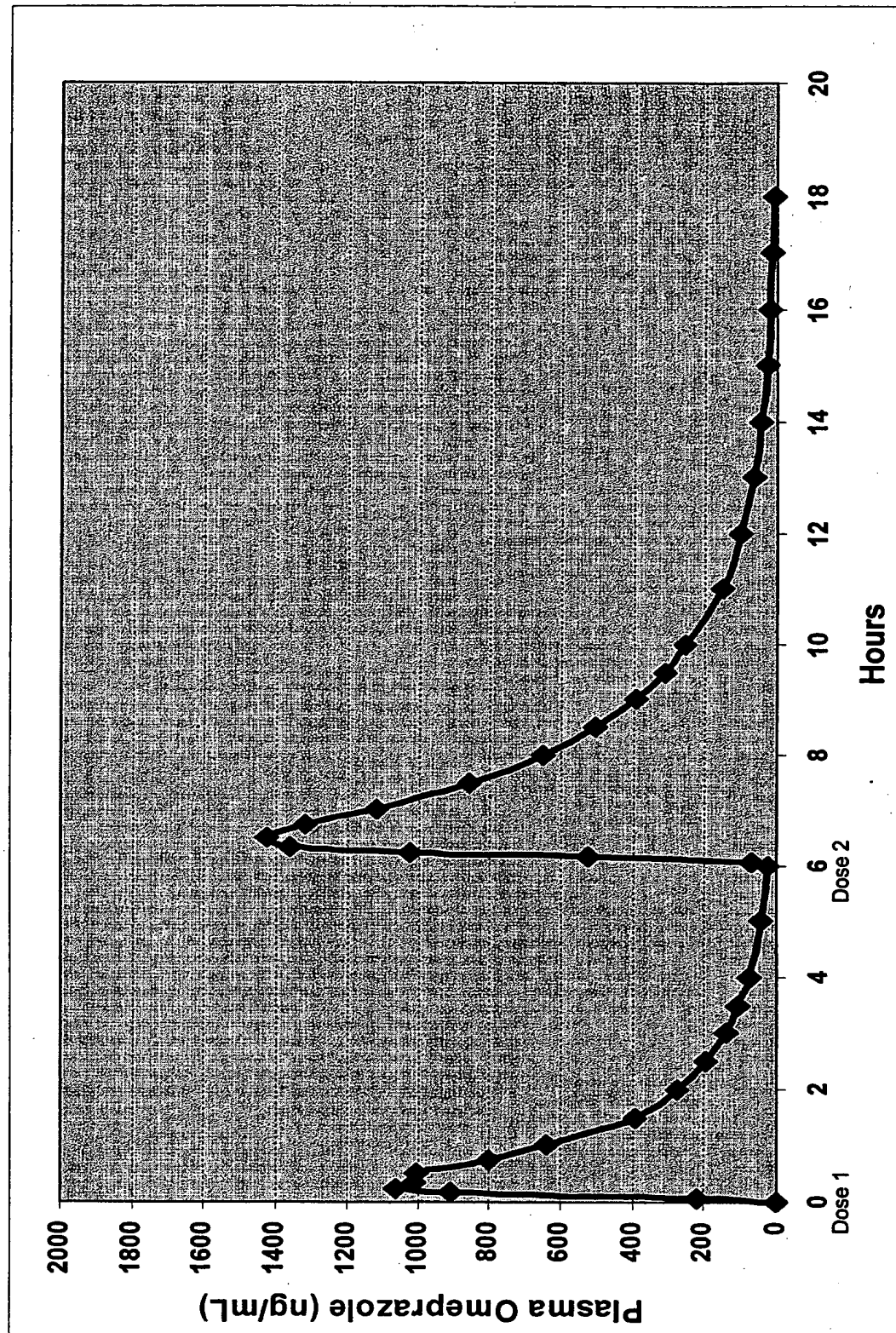
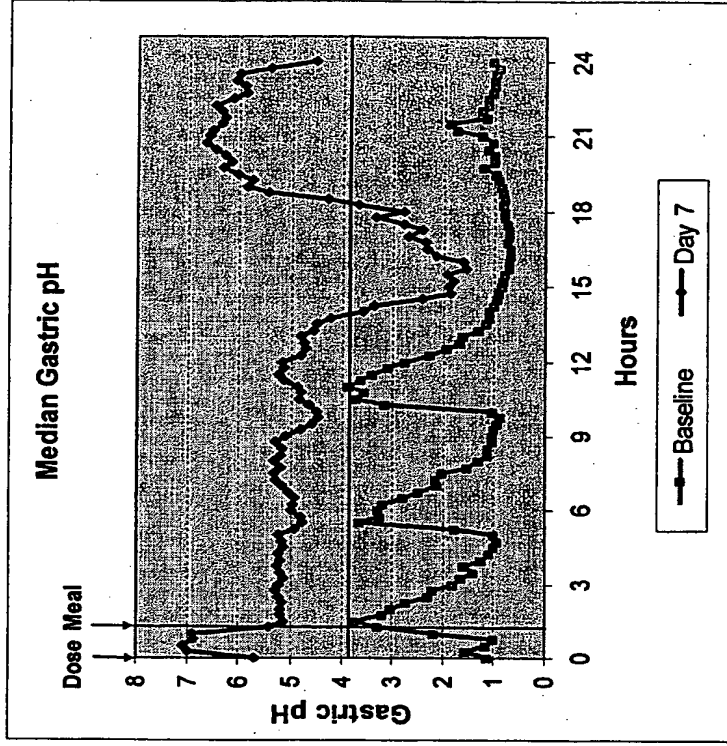
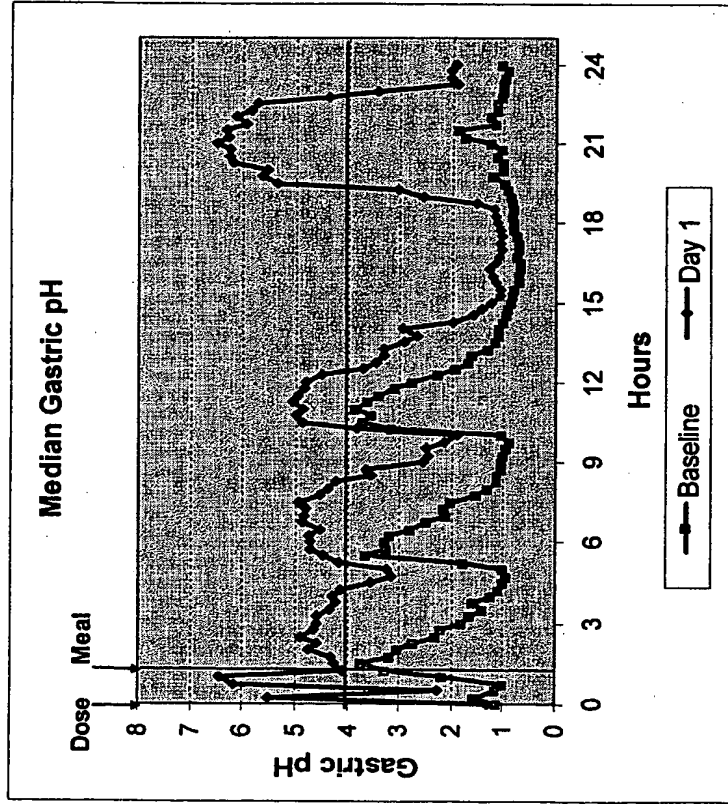


Figure 18A and Figure 18B

Median Gastric pH Over 24 Hours

After Administration of OSB-IR Suspension 40 mg qAM

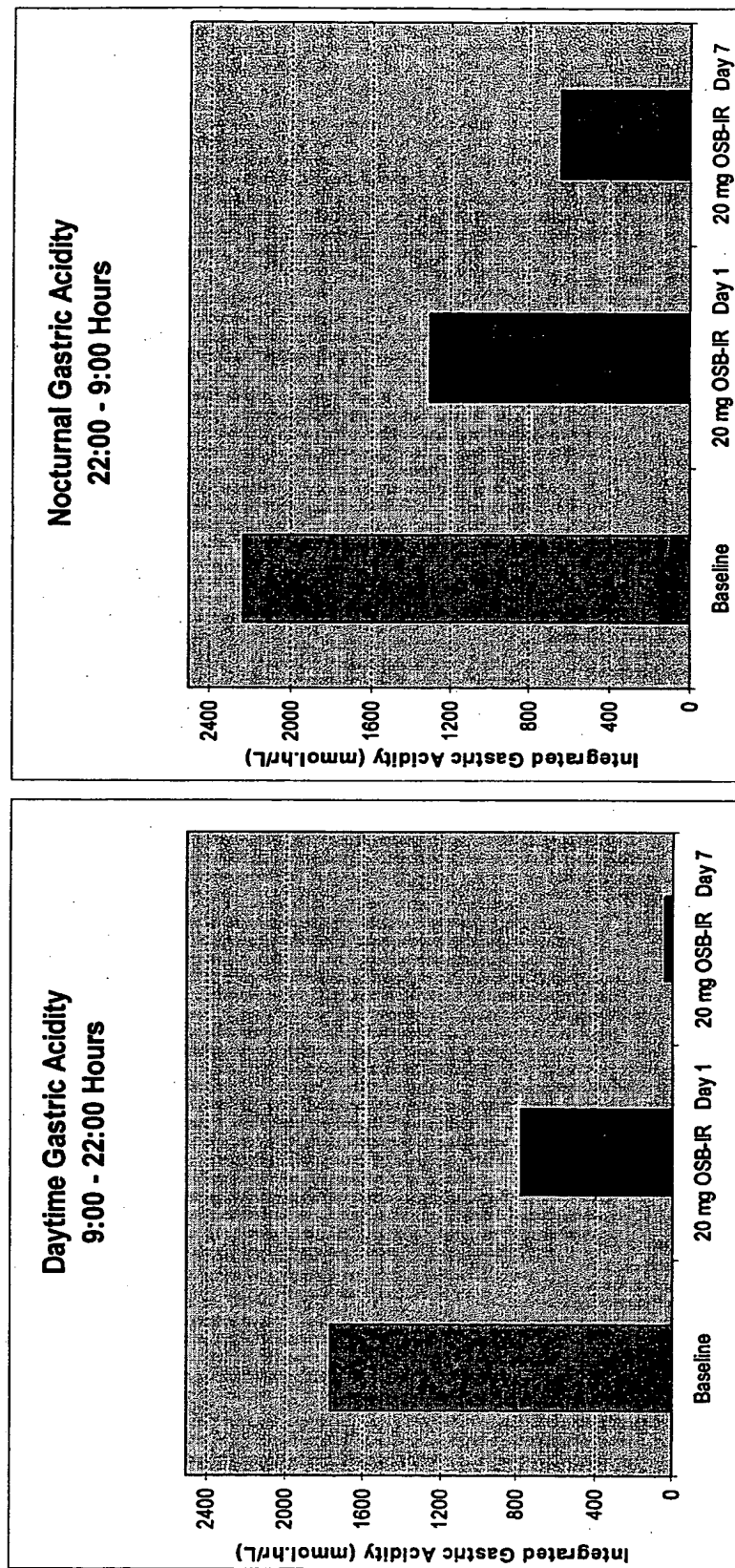


% Time pH > 4

Control	13%	- 3.1 hrs
OSB-IR 40 mg Day 1	47%	- 11.3 hrs
OSB-IR 40 mg Day 7	78%	- 18.7 hrs

OSB-IR-C02 (n=24)

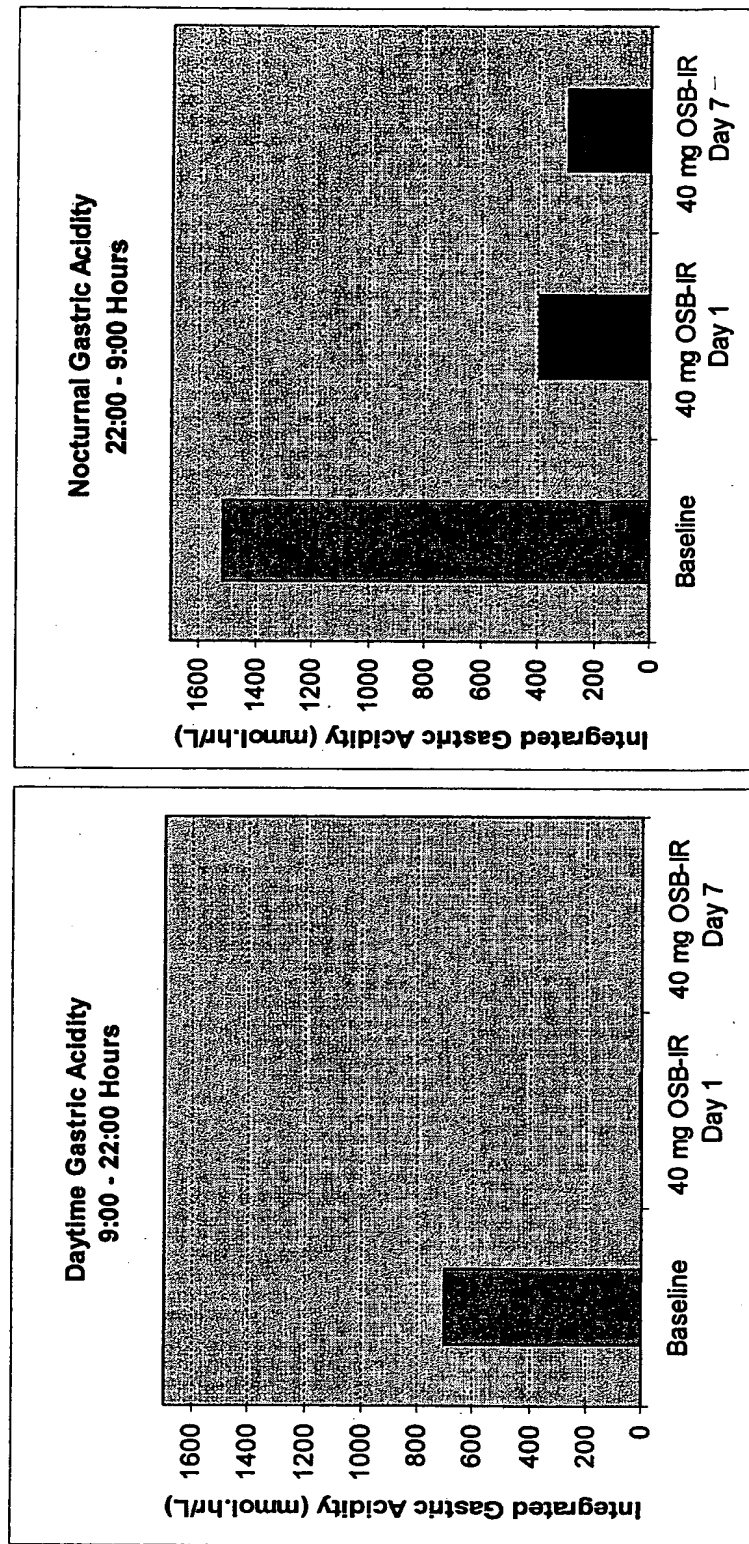
Figure 19A and Figure 19B  
 Effect of OSB-IR Suspension 20 mg on Daytime  
 and Nighttime Gastric Acidity



OSB-IR-C06 (n=28)

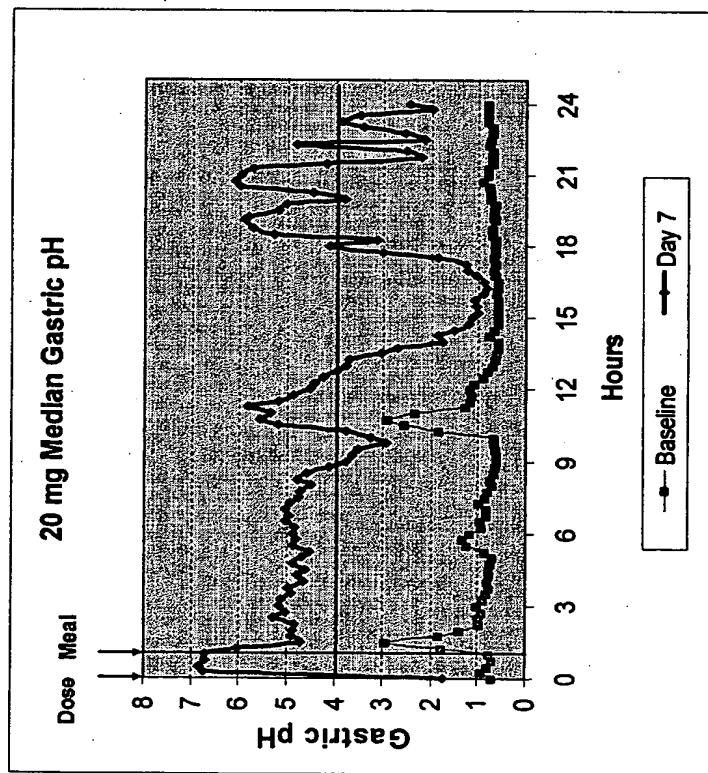


Figure 20A and Figure 20B  
Effect of OSB-IR Suspension 40 mg on Daytime  
and Nighttime Gastric Acidity



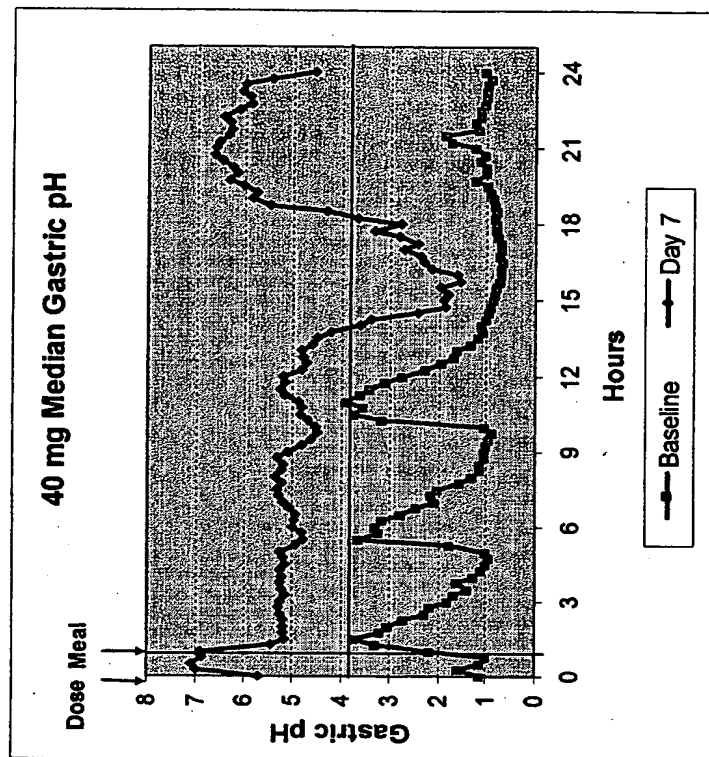
OSB-IR-C02 (n=24)

Figure 21A and Figure 21B  
Median Gastric pH Over 24 Hours After Administration  
Of OSB-IR Suspension (Steady State)



% Time pH > 4  
Control 4% - 1 hr  
OSB-IR 20 mg Day 7 50% - 12 hrs

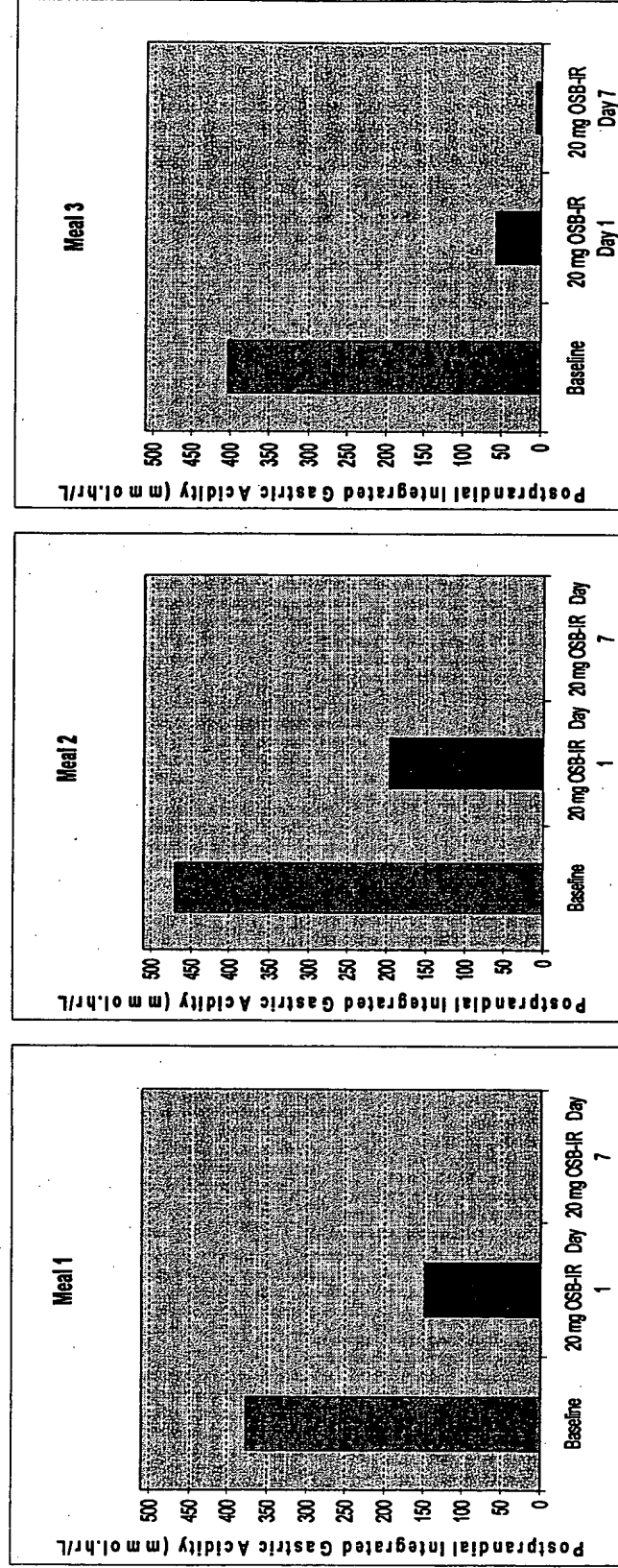
OSB-IR-C06 (n=28)



% Time pH > 4  
Control 13% - 3.1 hrs  
OSB-IR 40 mg Day 7 78% - 18.7 hrs

OSB-IR-C02 (n=24)

Figure 22A, Figure 22B, and Figure 22C  
 Effect of OSB-IR Suspension 20 mg on Postprandial  
 Integrated Gastric Acidity

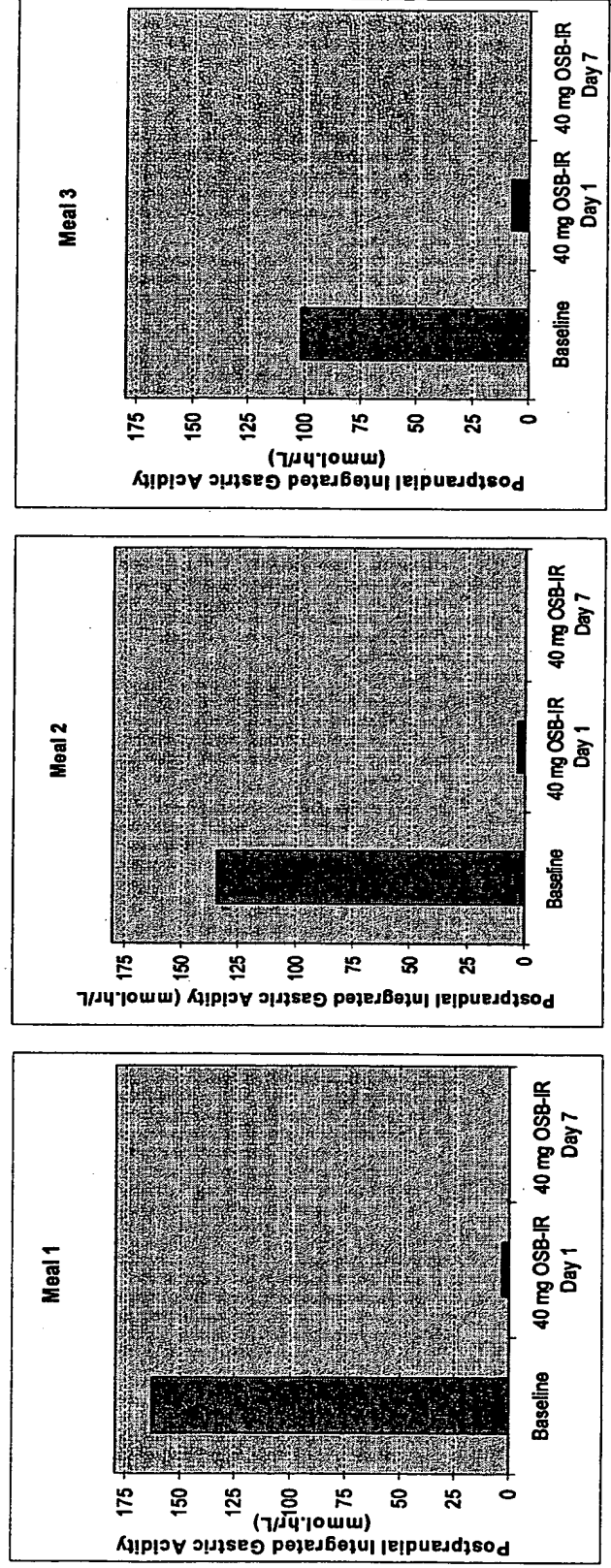


OSB-IR-C06 (n=28)  
 Postprandial period = 3 ½ hours from start of meal



Figure 23A, Figure 23B, and Figure 23C

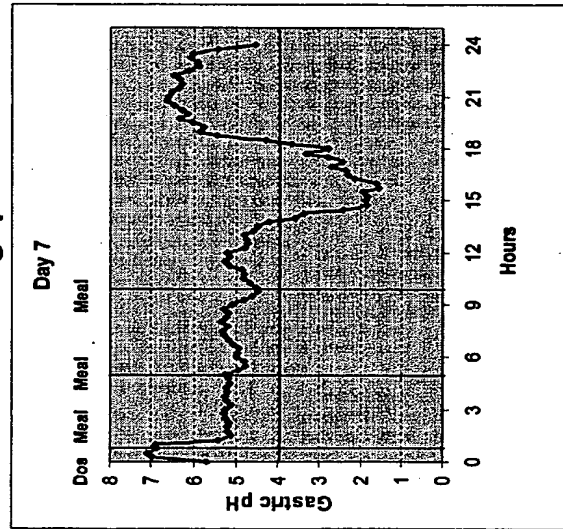
Effect of OSB-IR Suspension 40 mg on Postprandial Integrated Gastric Acidity



OSB-IR-C02 (n=24)  
 Postprandial period = 3 ½ hours from start of meal

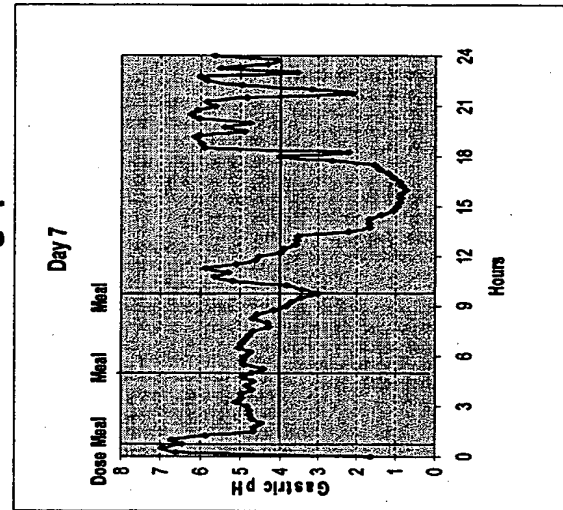
Figure 24A, Figure 24B, and Figure 24C  
Effect of Dosing Regimen on  
Median Gastric pH Over 24 Hours

40 mg qAM



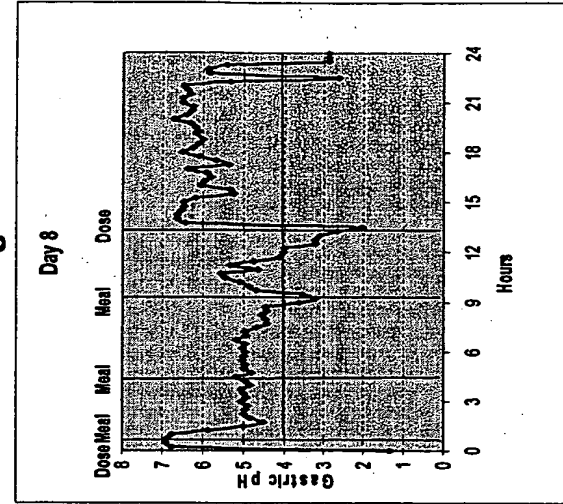
OSB-IR-C02

20 mg qAM



OSB-IR-C06

20 mg b.i.d.



OSB-IR-C06

% Time pH > 4 78%

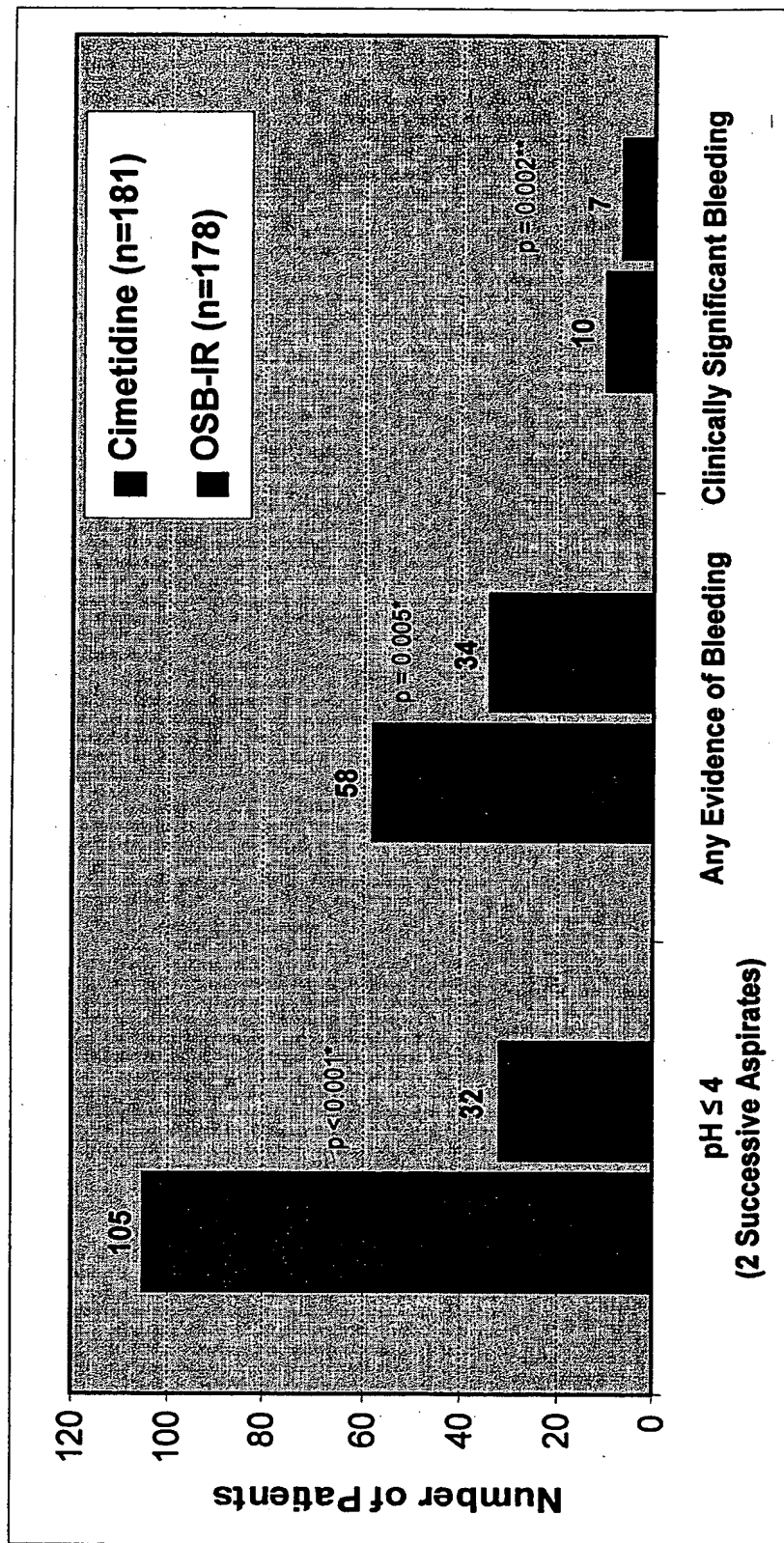
56%

79%

Note: Zero time is the 15-minute time interval prior to the time of dosing. Values are displayed for each 15-minute time interval of the 24-hour postdose recording period. Values are medians.

OSB-IR-C02 (n=24); OSB-IR-C06 (n=17)

Figure 25  
pH Control and Upper GI Bleeding  
In Critically Ill Patients



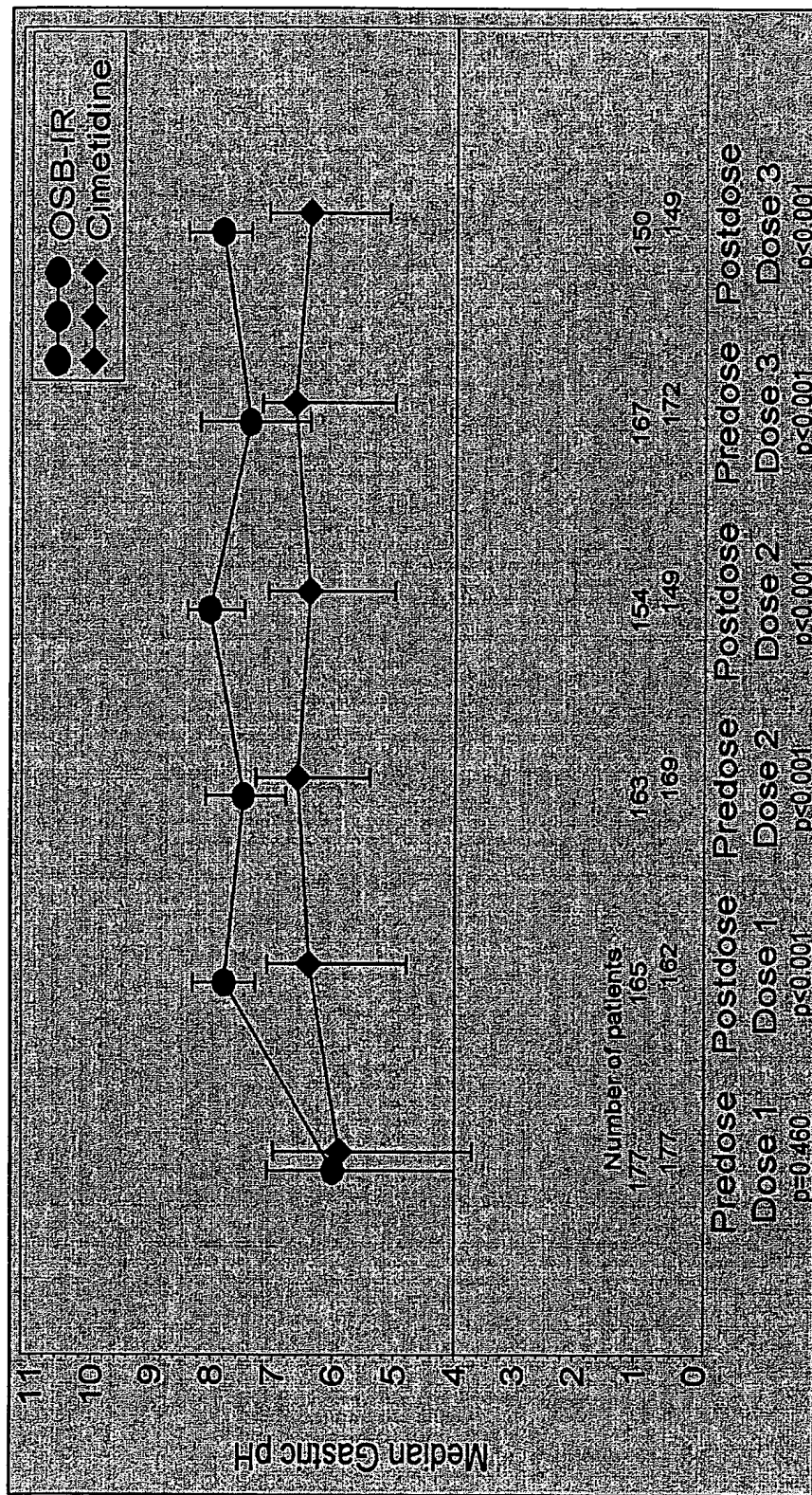
OSB-IR-C03 (n=359)

\* 2-sided Fisher's Exact test

\*\* 1-sided non-inferiority analysis

Figure 26

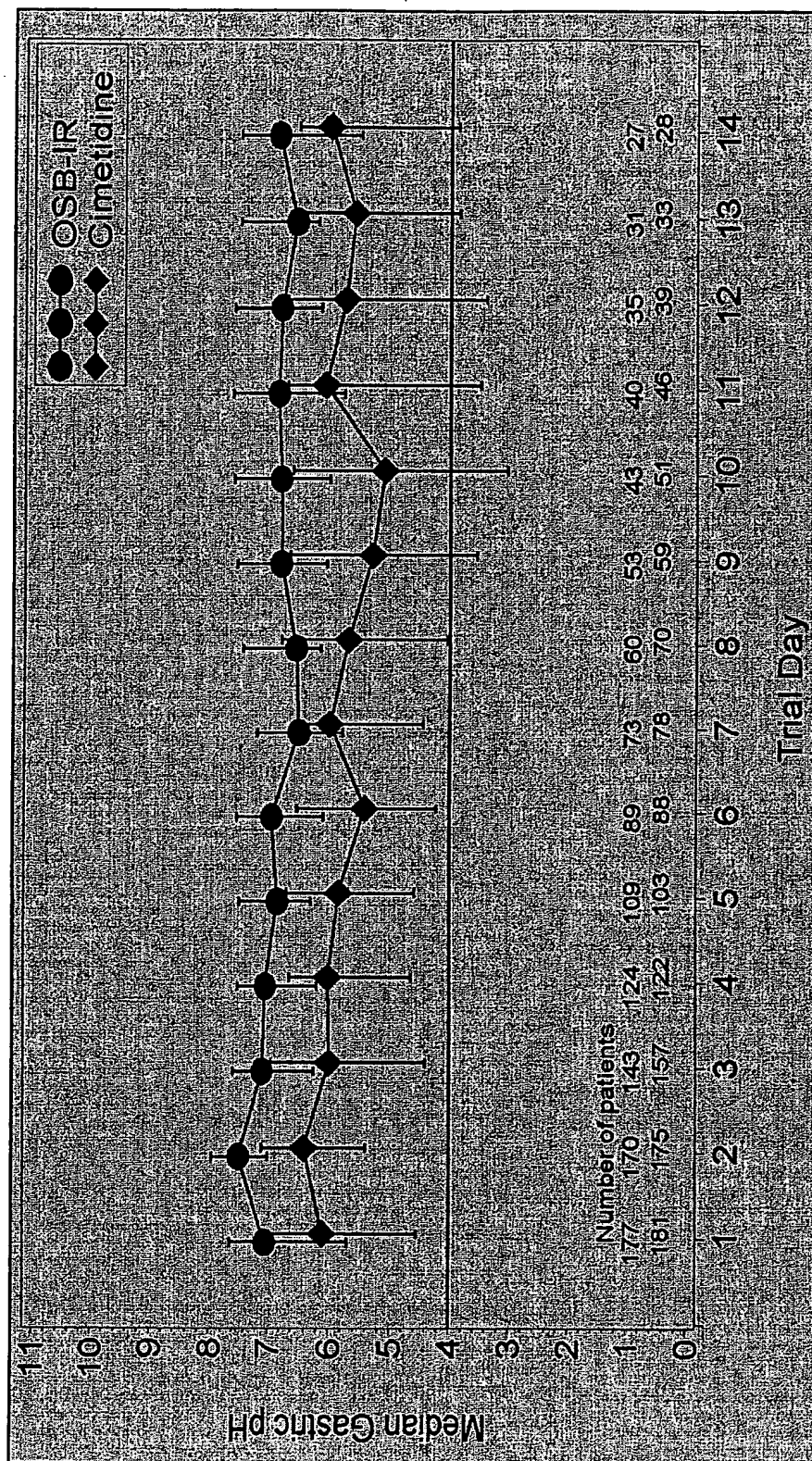
Median Gastric pH in Critically Ill Patients Dosed with OSB-IR Suspension 40 mg or IV Cimetidine  
(First Two Days of Dosing)



OSB-IR-C03 (n=359)

Predose samples obtained immediately before dosing; postdose samples obtained one hour after dosing. P-values were not adjusted for multiple comparisons. The median gastric pH was calculated for each patient for each trial day. The median and the 25<sup>th</sup> and 75<sup>th</sup> percentiles of these by-patient medians are displayed here.

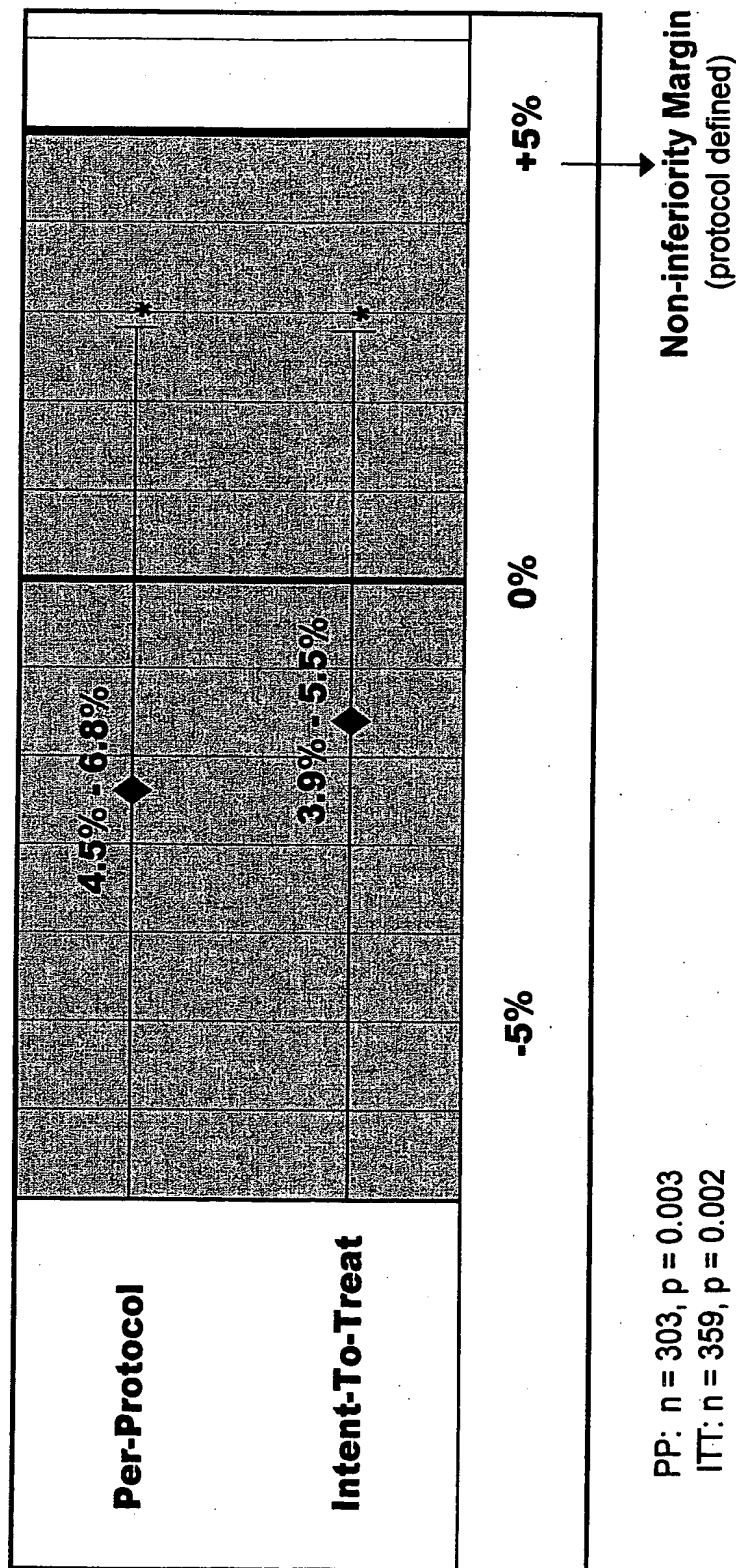
Figure 27  
Median Gastric pH in Critically Ill Patients Dosed with OSB-IR Suspension 40 mg or IV  
Cimetidine



OSB-IR-C03 (n=359)  
The median gastric pH was calculated for each patient for each trial day. The median and the 25<sup>th</sup> and 75<sup>th</sup> percentiles of these by-patient medians are displayed here.



Figure 28  
 Non-inferiority Analysis for  
 the Difference in Bleeding Rates  
 (OSB-IR Bleeding Rate minus Cimetidine Bleeding Rate)



PP: n = 303, p = 0.003

ITT: n = 359, p = 0.002

\* Boundary of one-sided 97.5% confidence interval.